REMARKS

Claims 11, 13-15, 17-26, and 71-81 are pending in the subject U.S. patent application and have been examined.

The United States Patent and Trademark Office (hereinafter the "Patent Office") has objected to the specification upon the assertion that the abstract of the disclosure is not descriptive of the claimed subject matter and is not in proper English, based on the contention that the present abstract is a sentence fragment. However, this objection has been held in abeyance until such time as claims are deemed to be in condition for allowance.

Claims 22 and 79 have been objected to on formal bases.

Claims 11, 13-15, 17-26, and 71-81 have been rejected under 35 U.S.C. § 101 upon the contention that the claimed invention is not supported by either a substantial asserted utility or a well-established utility.

Claims 11, 13-15, 17-26, and 71-81 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that since the claimed invention is not supported by either a substantial utility or a well established utility, one of skill in the art would not know how to make and use the claimed invention.

Claims 11, 13-15, 17-26, and 71-81 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed.

Claims 11, 14, 21, 24, 25, 71, 74, and 81 have been rejected under 35 U.S.C. § 112, second paragraph, upon the contention that the claims are indefinite.

Claims 14, 22, 24-26, 74, 79, and 81 have been amended. The amendments to claims 22, 26, and 79 are in response to informal objections, and thus do not include any new matter. The amendments to claims 14, 24, 25, 74, and 81 find support on page 27, lines 15-22 (examples of substantially identical nucleic acids). Thus, no new matter has been added as a result of the amendments to claims 14, 24, 25, 74, and 81.

Responses to the Claim Objections

Claims 22 and 79 have been objected to on formal bases. According to the Patent Office, the limitations "seeds" and "parts" appearing in claim 22 should by in the singular because a claim should be limited to a single invention. With respect to claim 79, the Patent Office asserts that the phrase "of claims" should read "claim" because the listed claims are presented in the alternative.

Turning first to the objection to claim 79, applicants respectfully submit that claim 79 has been amended to recite "claim". Applicants respectfully submit that the amendment to claim 79 is strictly to correct a grammatical error, and as such, is not to be interpreted as a surrender of any subject matter encompassed by the claim as originally presented.

With respect to claim 22, applicants have amended claim 22 to recite a seed, part, or progeny of a transgenic plant as claimed in claim 21. Applicants respectfully submit that similar language is recited in claim 26, and claim 26 has been similarly amended. Applicants respectfully submit that the amendments to claims 22 and 26 to singularize "seeds" and "parts" is strictly for formal reasons, and applicants do not acquiesce that "seeds" and "parts" necessarily encompass multiple inventions. For example, applicants respectfully submit that more than one "seed" of the transgenic plant would still encompass the same subject matter as one "seed". Nonetheless, applicants respectfully submit that the amendments address the instant objection to claim 22.

Applicants further respectfully submit that they have amended claim 22 to depend from claim 21, which recites a transgenic plant. It is apparent that the dependency of claim 22 from claim 20 resulted from a typographical error. Accordingly, no new matter has been added by correcting the dependency of claim 22.

As a result of the amendments to claims 22 and 79, applicants respectfully submit that the objections to these claims have been addressed. Applicants further respectfully submit that these claims are now in condition for allowance, and respectfully solicit a Notice of Allowance to that effect.

Response to the Claim Rejection under 35 U.S.C. § 101

Claims 11, 13-15, 17-26 and 71-81 have been rejected upon the contention that the claimed invention is not supported by either a substantial asserted utility or a well-established utility. After careful consideration of the rejection and the Patent Office's bases therefor, applicants respectfully traverse the rejection and submit the following.

Initially, the Patent Office's attention is directed to Public Comment (19) concerning the Utility Guidelines and the Patent Office's response thereto, published in Volume 66 of the Federal Register on page 1096, and concerning homology-based assertions of utility. The Patent Office's response indicated that a fact dependent inquiry is required because "the commenters provide no scientific evidence that homology-based assertions of utility are inherently unbelievable or involve implausible scientific principles". 66 Federal Register at page 1096, *citing In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995).

According to the Utility Examination Guidelines printed in the Federal Register,

> a patent examiner must accept a utility asserted by an applicant unless the Office has evidence or sound scientific reasoning to rebut the assertion. The examiner's decision must be supported by a preponderance of the evidence... More specifically, when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient... The Office will take into account both the nature and the degree of the homology.

Utility Examination Guidelines at page 1096 (citations omitted and emphasis added). Applicants respectfully submit that the Patent Office has not provided evidence or sound scientific reasoning to rebut the assertion in the present specification that currently claimed nucleic acids encode functional polypeptides, nor is the Patent Office's decision supported by a preponderance of the evidence.

Applicants respectfully submit that the instant claims are directed, *inter alia*, to isolated and purified nucleic acid molecules encoding a soybean *rhg1* and SDS resistance gene. See Figure 3 of the subject U.S. patent application as filed. The gene is capable of conveying *Heterodera glycines*-infestation resistance or *Fusarium solani*-infection resistance to a non-resistant soybean germplasm, the gene located within a quantitative trait locus mapping to linkage group G and mapped by genetic markers of SEQ ID NOs:1-6, said gene located along said quantitative trait locus between said markers. Positional cloning methods were used to isolate genomic sequences in the chromosomal regions of Forrest that confers SCN/SDS resistance, as further described in Example 4 in the subject U.S. patent application as filed. Specifically, *rhg1* sequences were derived from BAC clones 21D9 and 73P6 of the Forrest *Bam*HI or *Hind*III BAC libraries. In some embodiments, the gene comprises the nucleotide sequence set forth as SEQ ID NO:13 (Figure 7A-7B of the subject U.S. patent application as filed). BLASTP analysis of the translation of the *rhg1* gene (Figure 7C of the subject U.S. patent application as filed), set forth as SEQ ID:14 shows high homology to GENBANK® Accession No. T46070 described as hypothetical protein T18N14.120 from *Arabidopsis thaliana* (Figure 7E-7F of the subject U.S. patent application as filed), homology to the rice Xa21 disease resistance gene encoding a leucine-rich repeat protein, and homology to the tomato CF-2 gene for resistance to *Cladosporium fulvus* (Figure 7D of the subject U.S. patent application as filed).

Applicants respectfully submit that the instant claims are also directed, *inter alia*, to isolated and purified nucleic acid molecules encoding a soybean *Rhg4* gene. The gene is capable of conveying *Heterodera glycines*-infestation resistance to a non-resistant soybean germplasm, the gene located within a quantitative trait locus mapping to linkage group A2 and mapped by the AFLP markers of SEQ ID NOs:6-12, the gene located along said quantitative trait locus between said markers. Preferably, the gene comprises a nucleotide sequence set forth as any one of SEQ ID NOs:16-19. Genes underlying quantitative traits, or genes with related function, such as disease resistance, are often organized in

clusters within the genome (*e.g.*, Staskawicz *et al.* (1995) *Science* 268:661-667). In the case of SCN/SDS resistance, previous studies by the co-inventors of the presently disclosed subject matter have suggested that the resistance trait in Forrest may be caused by four genes in a cluster with two pairs in close linkage or by a two-gene cluster with each gene displaying pleitropy (Meksem *et al.* (1999) *Theor Appl Genet* 99:1131-1142).

Thus, genomic DNA isolated and disclosed herein comprises multiple resistance gene sequences. Additional sequences derived from the SCN/SDS resistance locus are set forth as SEQ ID NOs:20-66. BLASTX analysis of these sequences reveals further homology to known proteins in other organisms. Of particular interest, BLASTX analysis of the sequences set forth as SEQ ID NOs:67-114 reveals that several of the disclosed sequences have homology to GENBANK® Accession No. T46070 described as hypothetical protein T18N14.120 from *Arabidopsis thaliana*, homology to the tomato CF-2 disease resistance genes encoding leucine-rich repeat proteins, and to the tomato CF-9 gene for resistance to *Cladosporium fulvus*. *See* Table 1 of the subject U.S. patent application as filed.

Applicants respectfully submit that when the Patent Office takes into account the nature and the degree of the homology between the claimed polypeptides and known disease resistance polypeptides as required in the Interim Examination Guidelines, it is clear that the assignment of function as recited in the present claims is based on a "reasonable correlation" between the homologies of the various proteins.

Additionally, SEQ ID NO:13 (Figure 7) teaches the utility of marker assisted selection. The underline sequence **TTGAGGGAAAAGAT** teaches the position of a primer that can be extended to score an SNP (C/A change). Section XVI and Table 3 of the subject U.S. patent application show use of a linked marker for this utility. Also, SEQ ID NOs:13 and 14 (Figure 7) show a coding region for the protein encoded by the gene found in soybean roots.

Further, within the presently disclosed sequences are many microsatellite sequences that can quickly be used by one of ordinary skill in the art viewing this

sequence. Eleven GENBANK® records AY858573-AY858583 provide eleven examples of this utility for Rhg1 and GENBANK® records AY858565-AY858572 provide eight examples of this utility for Rhg4. It is respectfully submitted that the instant U.S. patent application teaches to those of ordinary skill in the art the position of markers found within the Rhg1 gene.

The attached Information Disclosure Statement also includes an article by University of Illinois researchers Brucker *et al.* (2005) *Theor Appl Genet* 111:44-9. This article refers to the instant U.S. patent application, and the identification of *rhg1* in the instant U.S. patent application as teaching the position of *rhg1*. This article also discusses that Rhg1 alleles from soybean PI 437654 and PI 88788 respond differentially to isolates of *Heterodera glycines* in the greenhouse.

Another article in the attached Information Disclosure Statement describes the position of Rhg1 and the utility of the markers taught by the instant U.S. patent application. *See* Concibido *et al.* (2004) *Crop Science* 44:1121-1131. It is thus respectfully submitted that the instant U.S. patent application teaches to those of ordinary skill in the art the position of markers found within the Rhg1 gene.

The sequences of SEQ ID NOs:13 and 14 (Figure 7) show a coding region for one form (allotype) of the protein encoded by the gene found in soybean roots. Both a large 110 kd (831 amino acids) and smaller derivatives (60 kd, 453 amino acids) have been detected *in planta* by the present applicants. Post-translational processing by subtilisin has been inferred. The encoded protein does not start with ATG, but this is not uncommon in plants. Plant transformation experimentation can be a long process, but length does necessarily make the experimentation undue. Thus, a functional gene product would be apparent to one of ordinary skill in the art upon a review of the sequences and techniques disclosed in the instant U.S. patent application.

Furthermore, applicants respectfully submit that the guidance for identifying and isolating a nucleic acid encoding an SCN/SDS resistance polypeptide is sufficient, contrary to the contentions of the Patent Office on page 7 of the Official Action. Indeed, when taken together, Examples 3 and 4 clearly

demonstrate to the skilled artisan the identification and isolation of a nucleic acid encoding an SCN/SDS resistance polypeptide.

Claim 11 and dependent claims recite an *Rhg1* nucleic acid encoding a biologically active RHG1 protein. The present applicants have detected RHG1 protein by antibodies raised to polypeptides encoded by SEQ ID NO:9. These antibodies have detected RHG1 protein in two forms, each of which is increased in abundance in SCN infected roots.

Claim 23 and dependent claims recite a biologically active Rhg4 gene and RHG4 protein. From cloned DNA used from SEQ ID NOs:7-12 and 16-19, the RHG4 protein and gene and associated promoter have been shown to confer resistance to SCN in hairy roots transformed with the gene.

Referring again to the attached Information Disclosure Statement, Meksem *et al.* (2001) *Molecular Breeding* 7:63-71, teaches that molecules linked to Rhg1 can be used for marker assisted selection of resistance to SCN and SDS in a breeding program. Meksem *et al.* (2001) *Mol Gen Genomics* 265:207-214 teaches that molecules linked to Rhg4 can be used for marker assisted selection of resistance to SCN and SDS in a breeding program. *See also* Meksem *et al.* (2001) Theor. Appl.Genet. 103:710-717, which teaches that the nearer the marker is to the gene the more efficient the selection for resistance.

Further, Meksem *et al.* (1999) *Theor Appl Genet* 99:1131-1142 shows that resistance to SCN and SDS are so closely clustered to not be separated by the then available markers. Triwitayakorn *et al.* (2005) *Genome* 48:125-138 shows that resistance to SCN and SDS are so closely clustered as to not be separated even by the markers presented in the instant U.S. patent application. That the one molecule can provide dual resistance can be observed through plant transformation experimentation. Plant transformation experimentation can be a long process, but length does necessarily make the experimentation undue. Thus, a functional gene product would be apparent to one of ordinary skill in the art upon a review of the sequences and techniques disclosed in the instant U.S. patent application.

Further, fragments of resistant genes can be biologically active, and as such, "complete" sequences of genes are not strictly necessary. Domains of proteins have separate functions. In the case of Rhg1 and Rhg 4 these comprise protein phoshorylation domains, transmembrane domains, leucine rich repeat domains, dimerization domains and elicitor or other factor binding domains. The complementing molecule in a transgenic plant need only complement the activity of domain missing from the susceptible protein. Complementation can occur at the protein level or by homologous recombination at the DNA level. *See also* the attached Information Disclosure Statement, which lists Lee *et al.* (1990) *Plant Cell* 2:415-25 (genes can insert and rewrite a susceptible plant gene to the resistant form).

Also, Venkatesh *et al.* (2000) *Weed Technology* 14:156-160 teaches that purple deadnettle (*Lamium purpureum*), henbit (*Lamium amplexicaule*), field pennycress (*Thlaspi arvense*), shepherd's-purse (*Capsella bursa-pastoris*) can serve as hosts for *H. glycines*. SCN has a relatively broad host range, but its only major agronomic host crop is soybean. Riggs (1992) Host range. In Riggs and Wrather (eds.) Biology and Management of the Soybean Cyst Nematode, St. Paul, Minnesota: American Phytopathological Society pp. 107-114, reviewed published studies of alternative SCN hosts and compiled a list of 96 genera of Fabaceae (Leguminosae) and 50 genera representing 22 families of non-legumes that have been reported as alternate hosts of SCN. Most of those studies were conducted prior to 1970 using plant accessions and what is now classified as race 3 SCN from the southern and southeastern U.S. In more recent work, Wong and Tylka (1994) *Plant Disease* 78:365-367, reported that eight common weed species of the U.S. Corn Belt, including Canada thistle [*Cirsium arvense* (L.) Scop.], common cocklebur (*Xanthium strumarium* L.), eastern black nightshade (*Solanum ptycanthum Dunal* ex DC.), field bindweed (*Convolvulus arvensis* L.), common lambsquarters (*Chenopodium album* L.), redroot pigweed (*Amaranthus retroflexus* L.), velvetleaf [*Abutilon theophrasti* (L.) Medic.], and common sunflower (*Helianthus annuus* L.), were nonhosts of race 3 SCN in Iowa. Sortland and

MacDonald (1987) *Plant Disease* 71:23-27, had reported previously that redroot pigweed and common lambsquarters were nonhosts of race 5 SCN in Minnesota."

Clearly then the genes described have utility in providing resistance to other plant species. In view of Whitham *et al.*, Proc Natl Acad Sci U S A. 1996 93(16):8776-81, which shows that resistance genes from tobacco can work in tomato, applicants respectfully submit that utility is both well established and well asserted.

Finally then, the difference between resistant and susceptible RHG1 proteins is known to be at least 1 and not more than 6 of the amino acids shown in Figure 7, SEQ ID NOs:13 and 14. Similarly, the difference between resistant and susceptible RHG4 proteins is known to be at least 1 and not more than 6 of the amino acids shown in SEQ ID NOs:16 to 19. Therefore the instant U.S. patent application includes all the information needed by an artisan to select for resistant plants and generate resistant transgenic plants of soybean and at least 187 plant species.

Given the utility shown for a nucleic acid encoding an rhg1 polypeptide, applicants respectfully submit that claim 11, which in one embodiment recites such a nucleic acid, is directed to patentable subject matter within the meaning of 35 U.S.C. § 101. Applicants further respectfully submit that claim 71, which recites the production of a transgenic plant, also is directed to patentable subject matter. Claims 13-15 and 17-26 and 72-80 depend directly or indirectly from claims 11 and 71, respectfully, and thus are also directed to patentable subject matter.

For the reasons set forth herein above, claim 81 is also believed to in condition for allowance and such action is earnestly solicited.

Applicants therefore respectfully request that the rejection under 35 U.S.C. § 101 of claims 11, 13-15, 17-26 and 71-81 be withdrawn.

Response to the Claim Rejections under 35 U.S.C. § 112, First Paragraph

Response to the First Rejection

Claims 11, 13-15, 17-26, and 71-81 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that since the claimed invention is not supported by either a substantial utility or a well established utility, one of skill in the art would not know how to make and use the claimed invention. After careful consideration of this rejection and the Patent Office's bases for the rejection, applicants respectfully traverse the rejections and submit the following.

With respect to the first contention, it appears that the Patent Office is basing this rejection on the 35 U.S.C. § 101 rejection presented and discussed hereinabove. The Patent Office's attention is directed to that discussion, wherein applicants have fully addressed the utility rejection presented. That discussion is incorporated here by reference.

Additionally, SEQ ID NO:13 (Figure 7) teaches the utility of marker assisted selection. The underlined sequence, **TTGAGGGAAAAGAT**, teaches the position of a primer that can be extended to score an SNP (C/A change). Section XVI and Table 3 of the subject U.S. patent application show use of a linked marker for this utility. Also, SEQ ID NOs:13 and 14 (Figure 7) show an entire coding region for the protein encoded by the gene found in soybean roots.

Further, within the presently disclosed sequences are many microsatellite sequences that can quickly be used by one of ordinary skill in the art viewing them. Eleven GENBANK® records AY858573-AY858583 provide eleven examples of this utility for Rhg1 and GENBANK® records AY858565-AY858572 provide eight examples of this utility for Rhg4. It is respectfully submitted that the instant U.S. patent application teaches to those of ordinary skill in the art the position of markers found within the Rhg1 gene.

The attached Information Disclosure Statement also includes an article by University of Illinois researchers Brucker, Carlson, Wright, Niblack, and Diers B., in *Theor Appl Genet.* 2005 Jun;111(1):44-9. This article refers to the instant U.S. patent application, and the identification of *rhg1* in the instant U.S. patent

application as teaching the position of *rhg1*. This article also discusses that Rhg1 alleles from soybean PI 437654 and PI 88788 respond differentially to isolates of *Heterodera glycines* in the greenhouse. *See also* Triwitayakorn, K., Njiti. V.N., Iqbal, M.J., Yaegashi, S., Town, C., and Lightfoot, D.A., *Genome* 2005 Feb;48(1):125-38.

Another article in the attached Information Disclosure Statement describes the position of Rhg1 and the utility of the markers taught by the instant U.S. patent application. *See* Concibido, V.C., *et al.*, *Crop Science* 2004 44:1121-1131. It is thus respectfully submitted that the instant U.S. patent application teaches to those of ordinary skill in the art the position of markers found within the Rhg1 gene.

The sequences of SEQ ID NOs:13 and 14 (Figure 7) show the coding region for one form (allotype) of the protein encoded by the gene found in soybean roots. Both a large 110 kd (831 amino acids) and smaller derivatives (60kd, 453 amino acids) have been detected *in planta* by the present applicants. Post-translational processing by subtilisin has been inferred. The encoded protein does not start with ATG, but this is not uncommon in plants. Plant transformation experimentation can be a long process, but length does necessarily make the experimentation undue. Thus, a functional gene product would be apparent to one of ordinary skill in the art upon a review of the sequences and techniques disclosed in the instant U.S. patent application.

Furthermore, applicants respectfully submit that the guidance for identifying and isolating a nucleic acid encoding an SCN/SDS resistance polypeptide is sufficient, contrary to the contentions of the Patent Office on page 7 of the Official Action. Indeed, when taken together, Examples 3 and 4 clearly demonstrate to the skilled artisan the identification and isolation of a nucleic acid encoding an SCN/SDS resistance polypeptide.

Claim 11 and dependent claims recite an *Rhg1* nucleic acid encoding a biologically active RHG1 protein. The present applicants have detected RHG1 protein by antibodies raised to polypeptides encoded by SEQ ID NO:9. These

antibodies have detected RHG1 protein in two forms and to be increased in abundance in SCN infected roots.

Claim 23 and dependent claims recite a biologically active Rhg4 gene and RHG4 protein. From cloned DNA used from SEQ ID NOs:7-12 and 16-19, the RHG4 protein and gene and associated promoter have been shown to confer resistance to SCN in hairy roots transformed with the gene.

Referring again to the attached Information Disclosure Statement, Meksem *et al.*, 2001, *Molecular Breeding* 7:63-71, teaches that molecules linked to Rhg1 can be used for marker-assisted selection of resistance to SCN and SDS in a breeding program. Meksem *et al.*, 2001, *Mol Gen Genomics* 265:207-214 teaches that molecules linked to Rhg4 can be used for marker assisted selection of resistance to SCN and SDS in a breeding program. See also Meksem, Pantazopolous, *et al.*, 2001, Theor. Appl.Genet. 103:710-717, teaches that the nearer the marker is to the gene the more efficient the selection for resistance.

Further, Meksem *et al.*,1999 Theor. Appl. Genet. 99: 1131-1142 shows that resistance to SCN and SDS are so closely clustered so as to not be separated by the then available markers. Triwitayakorn *et al.*, 2005 Genome 48:125-138 shows that resistance to SCN and SDS are so closely clustered to not be separated even by the markers as presented in the instant U.S. patent application. That the one molecule can provide dual resistance can be observed through plant transformation experimentation. Plant transformation experimentation can be a long process, but length does necessarily make the experimentation undue. Thus, a functional gene product would be apparent to one of ordinary skill in the art upon a review of the sequences and techniques disclosed in the instant U.S. patent application.

Further, fragments of resistant genes can be biologically active, and as such, "complete" sequences of genes are not strictly necessary. Domains of proteins have separate functions. In the case of Rhg1 and Rhg 4 these comprise protein phoshorylation domains, transmembrane domains, leucine rich repeat domains, dimerization domains and elicitor or other factor binding domains. The

complementing molecule in a transgenic plant need only complement the activity of domain missing from the susceptible protein. Complementation can occur at the protein level or by homologous recombination at the DNA level. Se also the attached Information Disclosure Statement, which lists Lee, K.Y., Lund, P., Lowe, K., and Dunsmuir, P. *Plant Cell* 1990 May;2(5):415-25 (genes can insert and rewrite a susceptible plant gene to the resistant form).

Also, Venkatesh *et al.*, Weed Technology: 2000 Vol. 14, No. 1, pp. 156–160 teaches that purple deadnettle (Lamium purpureum), henbit (Lamium amplexicaule), field pennycress (Thlaspi arvense), shepherd's-purse (Capsella bursa-pastoris) can serve as hosts for *H. glycines*. SCN has a relatively broad host range, but its only major agronomic host crop is soybean. Riggs, R.D. 1992. Host range. In R. D. Riggs and J. A. Wrather, eds. Biology and Management of the Soybean Cyst Nematode. St. Paul, MN: American Phytopathological Society. pp. 107–114, reviewed published studies of alternative SCN hosts and compiled a list of 96 genera of Fabaceae (Leguminosae) and 50 genera representing 22 families of non-legumes that have been reported as alternate hosts of SCN. Most of those studies were conducted prior to 1970 using plant accessions and what is now classified as race 3 SCN from the southern and southeastern U.S. In more recent work, Wong and Tylka (1994) *Plant Disease* 78:365-367 reported that eight common weed species of the U.S. Corn Belt, including Canada thistle [*Cirsium arvense* (L.) Scop.], common cocklebur (*Xanthium strumarium* L.), eastern black nightshade (*Solanum ptycanthum Dunal* ex DC.), field bindweed (*Convolvulus arvensis* L.), common lambsquarters (*Chenopodium album* L.), redroot pigweed (*Amaranthus retroflexus* L.), velvetleaf [*Abutilon theophrasti* (L.) Medic.], and common sunflower (*Helianthus annuus* L.), were nonhosts of race 3 SCN in Iowa. Sortland and MacDonald (1987) *Plant Disease* 71:23-27 had reported previously that redroot pigweed and common lambsquarters were nonhosts of race 5 SCN in Minnesota."

Clearly then the genes described have utility in providing resistance to other plant species. In view of Whitham *et al.* (1996) *Proc Natl Acad Sci U S A* 93:8776-

81 that show resistance genes from tobacco can work in tomato that utility is both well established and well asserted.

Finally then, the difference between resistant and susceptible RHG1 proteins is known to be at least 1 and not more than 6 of the amino acids shown in figure 7, sequences 13 and 14. Similarly, the difference between resistant and susceptible RHG4 proteins is known to be at least 1 and not more than 6 of the amino acids shown in sequences 16 to 19. Therefore the instant U.S. patent application contained all the information needed by an artisan to select for resistant plants and generate resistant transgenic plants of soybean and at least 187 plant species.

For the reasons set forth herein above, claim 81 is also believed to in condition for allowance and such action is earnestly solicited.

In summary, applicants respectfully submit that the instant rejection of claim 11, 13-15, 17-26, and 71-81 has been addressed. Accordingly, applicants respectfully request the withdrawal of the instant rejection.

Response to the Second Rejection

Claims 11, 13-15, 17-26, and 71-81 have also been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. After careful consideration of the rejection and the Patent Office's bases therefore, applicants respectfully traverse the rejection and offer the following.

Applicants respectfully submit that the instant claims are directed, *inter alia*, to isolated and purified nucleic acid molecules encoding a soybean *rhg1* and SDS resistance gene. See Figure 3 of the subject U.S. patent application as filed. The gene is capable of conveying *Heterodera glycines*-infestation resistance or *Fusarium solani*-infection resistance to a non-resistant soybean germplasm, the gene located within a quantitative trait locus mapping to linkage group G and mapped by genetic markers of SEQ ID NOs:1-6, said gene located

along said quantitative trait locus between said markers. Positional cloning methods were used to isolate genomic sequences in the chromosomal regions of Forrest that confers SCN/SDS resistance, as further described in Example 4 in the subject U.S. patent application as filed. Specifically, *rhg1* sequences were derived from BAC clones 21D9 and 73P6 of the Forrest *Bam*HI or *Hind*III BAC libraries. In some embodiments, the gene comprises the nucleotide sequence set forth as SEQ ID NO:13 (Figure 7A-7B of the subject U.S. patent application as filed). BLASTP analysis of the translation of the *rhg1* gene (Figure 7C of the subject U.S. patent application as filed), set forth as SEQ ID:14 shows homology to GENBANK® Accession No. T46070 described as hypothetical protein T18N14.120 from *Arabidopsis thaliana* (Figure 7E-7F of the subject U.S. patent application as filed), homology to the rice Xa21 disease resistance gene encoding a leucine-rich repeat protein, and homology to the tomato CF-2 gene for resistance to *Cladosporium fulvus* (Figure 7D of the subject U.S. patent application as filed).

Applicants respectfully submit that the instant claims are directed, *inter alia*, to isolated and purified nucleic acid molecules encoding a soybean *Rhg4* gene. The gene is capable of conveying *Heterodera glycines*-infestation resistance to a non-resistant soybean germplasm, the gene located within a quantitative trait locus mapping to linkage group A2 and mapped by the AFLP markers of SEQ ID NOs:6-12, the gene located along said quantitative trait locus between said markers. Preferably, the gene comprises a nucleotide sequence set forth as any one of SEQ ID NOs:16-19. Genes underlying quantitative traits, or genes with related function, such as disease resistance, are often organized in clusters within the genome (*e.g.*, Staskawicz *et al.* (1995) *Science* 268:661-667). In the case of SCN/SDS resistance, previous studies by the co-inventors of the present invention have suggested that the resistance trait in Forrest may be caused by four genes in a cluster with two pairs in close linkage or by a two-gene cluster with each gene displaying pleitropy (Meksem *et al.* (1999) *Theor Appl Genet* 99:1131-1142). Thus, genomic DNA isolated and disclosed herein comprise multiple resistance gene sequences. Additional sequences derived

from the SCN/SDS resistance locus are set forth as SEQ ID NOs:20-66. BLASTX analysis of these sequences reveals further homology to known proteins in other organisms. Of particular interest, BLASTX analysis of the sequences set forth as SEQ ID NOs:67-114 reveals that several of the disclosed sequences have homology to GENBANK® Accession No. T46070 described as hypothetical protein T18N14.120 from *Arabidopsis thaliana*, homology to the tomato CF-2 disease resistance genes encoding leucine-rich repeat proteins, and to the tomato CF-9 gene for resistance to *Cladosporium fulvus* . *See* Table 1 of the subject U.S. patent application as filed.

Thus, in the instant specification, the biomolecule is not described solely by a functional characteristic. Sequence data for the genes themselves is also included. Applicants further respectfully submit that between SEQ ID NO: 13, which corresponds to *Rhg1* and any one of SEQ ID NOs: 16-19, which correspond to *Rhg4*, there is over 98% sequence identity. Applicants submit that one of ordinary skill in the art would recognize that there is a disclosed correlation between the function described and the structure of the sequence.

The Patent Office also previously acknowledged that the specification describes AFLP markers associated with the soybean *Rhg4* gene at linkage group A2 mapped by AFLP markers. Applicants respectfully submit, however, that SEQ ID NOs: 16-19 disclose soybean *Rhg4*. Applicants respectfully submit that given the teachings of the instant specification in conjunction with the soybean *Rhg4* gene sequences explicitly disclosed in SEQ ID NOs: 16-19, it would have been apparent to the ordinary artisan that applicants were in possession of the claimed subject matter.

Further, fragments of resistant genes can be biologically active, and as such, "complete" sequences of genes are not strictly necessary. Domains of proteins have separate functions. In the case of Rhg1 and Rhg 4 these comprise protein phoshorylation domains, transmembrane domains, leucine rich repeat domains, dimerization domains and elicitor or other factor binding domains. The complementing molecule in a transgenic plant need only complement the activity of domain missing from the susceptible protein. Complementation can occur at

the protein level or by homologous recombination at the DNA level. *See also* the attached Information Disclosure Statement, which lists Lee *et al.* (1990) *Plant Cell* 2:415-25 (genes can insert and rewrite a susceptible plant gene to the resistant form).

Finally then, the difference between resistant and susceptible RHG1 proteins is known to be at least 1 and not more than 6 of the amino acids shown in figure 7, sequences 13 and 14. Similarly, the difference between resistant and susceptible RHG4 proteins is known to be at least 1 and not more than 6 of the amino acids shown in sequences 16 to 19. Therefore this patent application contained all the information needed by an artisan to select for resistant plants and generate resistant transgenic plants of soybean and at least 187 plant species.

Accordingly, applicants respectfully submit that the rejection of claims 11, 13-15, 17-26, and 71-81 under 35 U.S.C. § 112, first paragraph, has been addressed. Applicants further submit that the claims are in condition for allowance at this time, and respectfully request a Notice of Allowance to that effect.

Response to the Claim Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 11, 14, 21, 24, 25, 71, 74, and 81 have been rejected under 35 U.S.C. § 112, second paragraph, upon the contention that the claims are indefinite. According to the Patent Office, these claims are indefinite because there is nothing in the teachings of the instant application that demonstrates that a single resistance polypeptide can have biological activity against soybean cyst nematode infestation and sudden death syndrome (SCN/SDS). The Patent Office further asserts that the phrase "substantially identical to" appearing in claims 14, 24, 25, 74, and 81 renders these claims indefinite.

After careful review of the rejections and the Patent Office's bases therefor, applicants respectfully traverse the rejections and submit the following remarks.

With respect to the phrase "substantially identical to" in claims 14, 24, 25, 74, and 81, applicants respectfully submit that page 27 of the instant specification

specifically defines "substantially identical". However, in an effort to facilitate the instant prosecution, applicants have amended the rejected claims to replace "substantially identical to" with "at least 90% identical to". Support for the amendments can be found on page 27 of the instant specification. Applicants respectfully submit that the amendments to claims 14, 24, 25, 74, and 81 address the instant rejection.

Turning now to the rejection of claims 11, 14, 21, 24, 25, 71, 74, and 81, applicants respectfully submit that the Patent Office has not identified any terms or phrases that appear in these claims that would lead one of ordinary skill to misunderstand the metes and bounds of the claims. The specification as filed, for example, discloses that rhg1 "is capable of conveying *Heterodera glycines*-infestation resistance or *Fusarium solani*-infection resistance to a non-resistant soybean germplasm" (*see* Specification at page 39, line 24, to page 40, line 2). Page 40, line 22, through page 41, line 3, of the instant specification discloses that Rhg4 also has this activity.

Thus, applicants respectfully submit that the Patent Office has not provided a prima facie showing to support a rejection under 35 U.S.C. § 112, second paragraph. Accordingly, applicants respectfully submit that the instant rejection of claims 11, 14, 21, 24, 25, 71, 74, and 81 is improper, and respectfully request that it be withdrawn at this time.

Summarily, applicants respectfully submit that the rejections of claims 11, 14, 21, 24, 25, 71, 74, and 81 under 35 U.S.C. § 112, second paragraph, have been addressed, and respectfully request that they be withdrawn at this time. Applicants further respectfully submit that claims 11, 14, 21, 24, 25, 71, 74, and 81 are in condition for allowance, and respectfully solicit a Notice of Allowance to that effect.

CONCLUSIONS

As a result of the amendments to the specification and claims and the remarks provided herein, applicants respectfully submit that claims 11, 13-15, 17-26, and 71-82 are in condition for allowance. Applicants respectfully request a

Notice of Allowance to that effect. Should there be any minor issues outstanding in this matter, Examiner Kruse is respectfully requested to telephone the undersigned attorney. Early passage of the subject application to issue is earnestly solicited.

Deposit Account

The Commissioner is hereby authorized to charge any deficiency or credit any overpayment associated with the filing of this correspondence to Deposit Account Number **50-0426**.

Respectfully submitted,

JENKINS, WILSON & TAYLOR, P.A.

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